WHITE MATTER MICROSTRUCTURE IN RELATION TO READING PROFICIENCY AND BEHAVIORAL INATTENTION

A Dissertation

Presented to

The Faculty of the Department of Psychology

University of Houston

In Partial Fulfillment

of the Requirements for the Degree

Doctorate of Psychology

By

C. Nikki Arrington

May, 2015

WHITE MATTER MICROSTRUCTURE IN RELATION TO READING PROFICIENCY AND BEHAVIORAL INATTENTION

An Abstract of a Dissertation

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Abstract

Components of reading proficiency such as accuracy, fluency, and comprehension require the successful coordination of numerous, yet distinct, cortical regions. Underlying white matter tracts such as the arcuate fasciculus, inferior fronto-occipito fasciculus, inferior longitudinal fasciculus, and uncinate fasciculus allow for the communication among these regions. This study utilized unique full tract versus residualized tract–based spatial statistics methodology to identify the relations of white matter microstructure integrity to word reading proficiency, as well as behavioral inattention, in poor readers and typical school-aged readers. I hypothesized that white matter integrity would be differentially related to behavioral inattention and reading proficiency in poor versus typical readers, with increased integrity positively associated with increased reading proficiency and negatively associated with behavioral inattention. Results indicated measures of white matter integrity were differentially associated with reading proficiency and behavioral inattention. The right arcuate was positively correlated with accuracy and fluency in typical readers. Comprehension was negatively correlated with left uncinate. Reading accuracy was negatively correlated with right inferior longitudinal and bilateral arcuate in poor readers. Comprehension and fluency were positively correlated with left inferior longitudinal and right uncinate, respectively. Behavioral inattention was positively correlated with right inferior fronto-occipito and uncinate in typical readers. These findings expand our knowledge of the association between white matter integrity and different elements of reading proficiency and behavioral inattention.

Keywords: reading proficiency; behavioral inattention; white matter; DTI

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"To all the remarkable,
maddening, challenging,
frustrating people who inspire us
to do great things."
~ Richard Castle

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Table of Contents

White Matter Microstructure in Relation to Reading Proficiency and Behavioral Inattention

Reading is not an innate cognitive ability. Instead it is a learned representation of language in written form, specific to humans. This form of communication allows for the processing of orthographic symbols in order to extract meaning from text so that communication is not restricted to oral language.

Both reading and writing constitute a means for representing language in a physical environment. A metacognitive awareness of the internal structures of speech is essential for the ability to assess and make sense of written language. In an alphabetic language system, such as English, phonemes (i.e., constituent sound parts that make a difference in the meaning of a word) play an integral part in both visual and verbal forms of communication (Adams, 1990). Phonemes can be combined to form a variety of morphemes, the smallest combination of speech sounds that portray meaning (e.g. non- or -ing), that are then linked together to form words, which we consider as the meaningful basis of language. By mapping phonemes onto visual symbols (i.e. letters), text-based representations known as graphemes become the basis for reading and writing development. Learning the correspondence of graphemes to phonemes provides the foundation from which the reader is able to form a working knowledge of the relationship between text and speech sounds.

As the developing reader is exposed to print he or she acquires a mental framework for representing the relation between text and speech that allows for subsequent mastery of word recognition and spelling. This framework is connected via the phonological lexicon which stores the auditory sound form of words (i.e., phonemes); the sematic lexicon which stores the meaning of words; and the orthographic lexicon, which is responsible for storing the visual representation of words (Frith, 1985).

The development of a semantic and phonological lexicon is a spontaneous process that develops with the exposure to language (Frith, 1985). On the other hand, the development of an orthographic lexicon is dependent on explicit exposure to print and instruction. Although word recognition increases rapidly with adequate phonological awareness, reading comprehension and fluency/automaticity skills are acquired more gradually with increased exposure to print and reading practice. Most children develop accurate and fluent reading skills; however, 6-17% of children struggle with reading proficiency even after exposure to standard didactic instruction and appropriate opportunities to learn (Vellutino, Fletcher, Snowling, & Scanlon, 2004).

Learning to read is not trivial and places a high demand on cognitive resources. It also requires a great deal of reorganization in the brain because it is not “hardwired” for such tasks (Dehaene, 2009). Instead, the brain utilizes other preliteracy sources such as those allocated for vision and language (Vogel, Peterson, & Schlaggar, 2014). Proficient reading requires the successful utilization and coordination of a number of cognitive processes that facilitate a coherent representation of text. This implies that reading requires not only the successful activation of multiple, relevant brain regions but also adequate communication between these areas.

Dual Route Models of Reading

According to dual route models of reading there are two routes involved in the reading process: one corresponding to the semantic and phonological lexicon, the other to the orthographic lexicon (Coltheart, 1985). While several variants of the dual model exist, all incorporate the idea of multiple reading routes (Colheart, Curtis, Atkins, & Haller, 1993; Coltheart, Rastle, Perry, Langdon & Zigler, 2001; Dehaene, 2009). Structural and functional magnetic resonance imaging (MRI) studies have investigated neural structures associated with the dual route, identifying several brain regions that operate as a network underlying reading ability. These regions typically operate as a predominantly left-hemispheric network of inferior frontal, temporoparietal, and occipitotemporal cortical regions (Vandermosten, Boets, Wouters, & Ghesquiere, 2012b). Two distinct neural routes, or systems, have been shown to be involved: the dorsal phonological system and the ventral orthographic system. These systems work, in parallel, to accomplish fluent and proficient reading.

Phonological route. The dorsal *phonological system* is comprised of both the left temporoparietal junction as well as frontal regions in and around the inferior frontal gyrus (Broca's area). This primary system is typically associated with phonological decoding or word reading.

Lesions to the phonological route can lead to deficits in phonological decoding. Functional neuroimaging studies suggest that poor word reading skills are associated with reduced activation patterns in regions of the phonological system such as the posterior temporoparietal cortex (Eden & Zeffiro, 1998). Children and adults with poor word reading skills have been shown to have significantly reduced activation in the left temporoparietal cortex during real word and pseudoword reading tasks, as compared to those without reading difficulties (Brunswick, McCrory, Price, Firth, & Firth, 1999; Shaywitz et al, 2002). Farris et al. (2011) found that performance on pseudoword and real word reading measures increased in relation to functional connectivity within the frontal cortex in a group of children, with and without reading difficulties. Additionally, a longitudinal study of typically developing children showed cortical thickening in the left inferior frontal region was associated with greater development of phonological processing skills (Lu et al., 2007).

Orthographic route. In contrast to the dorsal phonological system, the ventral *orthographic system* is typically associated with the left occiptiotemporal sulcus (Visual Word Form area) which is typically linked to the automatic processing of visual word form perception that is necessary for reading fluency (Cohen et al., 2000, 2002). More recent research indicates that while this region is particularly useful for reading, it is necessary for any task that requires general processing (Vogel et al., 2014). Through connections with semantic areas such as those in portions of the inferior temporal and middle temporal gyrus as well as the inferior frontal gyrus, the Visual Word Form area supports automatized word recognition based on orthographic patterns the brain learns to recognize through continued exposure (Vandermosten et al., 2012b).

Damage to the orthographic route contributes to a different type of impairment in which phonological decoding remains intact but difficulties arise when attempting to read irregular words, such as “ache” or “enough,” that require more rote memorization because they do not follow standard orthographic to phonemic conversion rules. In one study, a participant with a lesion to the left ventral occipitotemporal sulcus showed no significant difference in phonological decoding ability compared to controls (Seghier, 2012). Instead, reading difficulties were more apparent when presented with words that did not adhere to typical rules of orthographic–phonemic conversion. Structural imaging studies have identified reduced gray matter volume in bilateral occipitotemporal cortex in individuals with similar reading difficulties (Kronbichler et al., 2008). Functional imaging studies have also shown consistent activation of brain regions associated with the orthographic system, such as the left occipitotemporal sulcus, during reading tasks requiring lexical decision making (Jobard, Crivello, & Tzourio-Mazoyer, 2003).

Given that reading constitutes a complex coordination of cognitive processes, it is not surprising that it utilizes numerous, yet distinct, cortical regions. To the extent that different reading processes require differing sets of those processes, then it may also follow that word reading, reading fluency, and reading comprehension skills have some overlap in neural correlates. The pattern of correlates may also vary across development, as skill develops and more basic skills become automated and newer, more complex skills must be mastered. Not only does proficient reading require adequate activation of relevant cortical areas, it also requires successful communication among these areas. Given this, there may be a connection between altered brain activity and the organization of white matter in poor readers.

Diffusion Tensor Imaging

Much is known about cortical regions involved in reading through lesion studies and through functional neuroimaging studies. However, equally intriguing is how these regions are connected. Diffusion tensor imaging (DTI) has allowed for the investigation of white matter tract integrity, including tracts associated with reading – related cortical regions. DTI is a noninvasive, *in vivo* MRI technique which estimates microstructural properties of white matter tracts by evaluating the diffusion of water molecules in and around nerve fibers (Mori & Zhang, 2006). White matter tracts are multidirectional and are composed of myelinated axons running parallel to one another. In these tracts, diffusion is greatest running parallel to the tract rather than perpendicular to it, a phenomenon known as anisotropic diffusion. One major advantage of DTI technology is that it is rotationally invariant, meaning that it allows for the measurement of principal diffusivities regardless of the positioning of white matter fibers (Assaf & Pasternak, 2008). DTI allows for evaluation of the direction and magnitude of water diffusion within white matter tracts, as well as providing a measure of track volume.

The use of DTI technology provides a framework for the acquisition, analysis, and quantification of the diffusion properties of white matter. Quantitative analysis yields many different diffusivity-based measures of white matter integrity with fractional anisotropy (FA) the most widely used (Assaf & Pasternak, 2008). The FA index utilizes eigenvalues that quantify diffusivity parallel and perpendicular to the fibers (also termed principal diffusivities) to measure the fraction of the “magnitude” of anisotropic diffusion (i.e. the normalized standard deviation of the diffusivities) (Assaf & Pasternak, 2008; Basser & Pierpaoli, 1996). This quantifies the degree of directionality of diffusivity and is used as an index of white matter integrity because it is determined by the degree of myelination and other properties of the axons (Mori, 2007). This measure provides a gray-scale, 2D map with intensity limits between zero and one. FA values are highest in white matter structures such as the corpus callosum and the ventral internal capsule, where anisotropy is highest, reflecting fast diffusivity parallel to fibers and slower diffusivity perpendicular to them (Assaf & Pasternak, 2008; Basser & Pierpaoli, 1996; Pierpaoli, Jezzard, Basser, Barnett, & Di Chiro, 1996). In gray matter and cerebral spinal fluid, FA values are lowest because diffusivity is similar in all directions, with anisotropy approaching zero. Therefore, when evaluating white matter tract integrity, it would be expected that higher FA values would be associated with higher integrity and therefore, increased behavioral performance. As a marker of white matter integrity, FA is a useful quantity to compare across subjects as it provides information about diffusion anisotropy differences, independent of fiber orientation (Pierpaoli & Basser, 1996).

White Matter Tracts Associated with Reading

Diffusion tensor methodology has permitted examination of the integrity of white matter pathways that have been linked to reading and language. Despite this, little is known about the relation of white matter integrity and reading achievement, particularly when differentiating the role of white matter tracts associated with word reading versus reading fluency and reading comprehension. Recent research has established an association between poor reading proficiency and poor white matter tract integrity in tracts such as the arcuate fasciculus (AF), inferior fronto - occipito fasciculus (IFOF), inferior longitudinal fasciculus (ILF), and the unicinate fasciculus (UF; Vandermosten et al., 2012b) (Figure 1). Research suggests that these tracts play a role in reading by contributing to word reading accuracy, word reading fluency, and/or overall reading comprehension but little is known about the distinct function of each.

Arcuate fasciculus. The AF, also commonly referred to as the superior longitudinal fasciculus, is a lateral associative white matter tract connecting the temporoparietal area with the inferior frontal gyrus (Catani & Thiebaut de Schotten, 2008). The left AF has been shown to be involved in language processing and is often associated with the phonological route of reading (Catani, Jones, & Ffytche, 2005; Catani & Thiebaut de Schotten, 2008). Catani et al. (2005) further segments the AF into three branches: (1) the AF – direct, a direct segment running medially, connecting the temporoparietal area and the inferior frontal gyrus; (2) the AF – indirect, the lateral, anterior segment which links the inferior frontal gyrus and the inferior parietal lobule; and (3) the AF – posterior which links the temporoparietal region with the inferior parietal lobule via the lateral indirect posterior segment.

Longitudinally, measures of white matter integrity (i.e. FA values) in the left AF have been shown to correlate with rate of reading development (Yeatman, Dougherty, Ben-Shachar, & Wandell, 2012). FA values in the AF have also been shown to be significantly correlated with measures of word reading accuracy (Frye et al., 2010; Hoeft et al., 2011; Lebel et al., 2013) and reading fluency (Lebel et al., 2013). Lebel et al. (2013) found FA values in parietal portions of the AF, bilaterally, where positively correlated with a measure of word reading fluency. Additionally, FA in the right AF was positively correlated with word reading accuracy, in a sample of typically developing adolescents and young adults. Hoeft et al. (2011) found that FA values in the left AF were significantly correlated with a measure of word reading accuracy in typical school – aged children. Similarly, children and adults with poor word reading ability have been shown to have significantly lower FA values in the left AF, which supports a link between it and phonological processing (Carter et al., 2009; Vandermosten et al., 2012a).

Inferior fronto-occipital fasciculus. The IFOF is an association bundle of white matter tracts which connects the ventral occipital lobe and the orbitofrontal cortex (Canati, Jones, & Ffytche, 2005). The role of the IFOF is poorly understood but research suggests it may function in tasks such as visual processing (Fox et al., 2008; Rudrauff et al., 2008), reading (Epelbaum et al., 2008; Catani & Mesulam, 2008), and attention (Doricchi et al., 2008). The IFOF may serve as the neuroanatomical correlate of the ventral orthographic reading route (Schlaggar & McCandliss, 2007; Vandermosten et al., 2012a).

Research suggests a role for the IFOF in multiple aspects of reading proficiency. Portions of the IFOF have been shown to correlate with measures of word reading accuracy (Feldman, Lee, Yeatman, & Yeom, 2012; Odegard, Farris, Ring, McColl, & Black, 2009) and reading fluency (Lebel et al., 2013). A strong positive correlation between pseudoword decoding and FA values in bilateral IFOF, was found in a study utilizing tract – based spatial statistics (TBSS), which maps individual DTI data onto a white matter 'skeleton' created from mean FA (Odegard et al., 2009). Conversely, Vandermosten et al. (2012a) found no significant difference in FA values of the left IFOF in adults with word reading difficulties compared to normal controls. In the same study, FA values of the left IFOF were significantly correlated with measures of orthographic processing but not phoneme awareness or speech perception. One study also reported a significant, moderate correlation between the right IFOF and reading comprehension. While research suggests the role of the IFOF as a pathway involved in the orthographic route of reading, findings are mixed.

Inferior longitudinal fasciculus. The ILF is a ventral associative tract which consists of a bundle of both long and short fibers directly connecting the occipital and anterior temporal lobes (Canati et al., 2005). While the function of this tract is not well understood, it is believed to mediate facial recognition (Fox et al., 2008), visual perception (Ffytche, 2008), and visual memory (Ross, 2008). The ILF is also believed to play a role in the ventral orthographic route of reading because of its connections from occipital areas to the Visual Word Form Area (Vandermosten et al., 2012b).

Research has suggested a relation between the ILF and measures of word reading fluency (Horowitz-Kraus, Wang, Plante, & Holland, 2014; Lebel et al., 2013) and reading comprehension (Feldman et al., 2012; Horowitz-Kraus et al., 2014). Feldman et al. (2012)

found FA values in bilateral ILF to be positively correlated with reading comprehension. A study utilizing TBSS methodology found FA values in the ILF to be significantly correlated with reading fluency, bilaterally (Horowitz-Kraus et al., 2014). In a fiber tracking study of an individual with acquired alexia, Epelbaum et al. (2008) reported that the onset of alexia without agraphia began after the previously intact ILF degraded after surgery. They concluded that the ILF is responsible for conveying low level visual information from occipital areas to the Visual Word Form Area for orthographical processing.

Uncinate fasciculus. The UF is a ventral association bundle considered to be part of the limbic system. It interconnects the anterior temporal lobe with the orbitofrontal cortex, including the inferior frontal gyrus (Catani et al., 2002). The function of the UF is poorly understood but it is believed to be involved in emotion processing and memory (Gaffan & Wilson, 2008). Additionally, it is thought to play a role in language functions such as lexical retrieval and semantic associations (Catani & Mesulam, 2008). Portions of this tract connecting the temporal and frontal components of the language network may account for the significant relation between the right UF and measures of verbal working memory and comprehension (Nester et al., 2013). One study reported a significant correlation between a measure of reading comprehension and the UF, bilaterally, in a group of preterm and typically developing children and adolescents (Feldman et al., 2012). These findings suggest a role of the UF in reading comprehension but further research is needed to identify the relation of the UF and components of reading proficiency.

In sum, neuroimaging research indicates the importance of a left – hemispheric network of inferior frontal, temporal, and occipitotemporal cortical regions in reading, with connecting white matter tracts playing a vital role in communication between these regions. Little is known about how the integrity of these tracts impacts reading proficiency.

Behavioral Inattention and Reading Disability

White matter tract integrity as it relates to reading proficiency is complicated by the frequent presence of comorbid disorders such as conduct disorder or attention deficit – hyperactivity disorder (ADHD). Comorbidity refers to the co-occurrence of more than one psychological disorder in the same individual. Research indicates that approximately 60% of children with a diagnosed reading disability also meet criteria for at least one additional disability (Carroll, Maughan, Goodman, & Meltzer, 2005; Willcutt & Pennington, 2000). The prevalence of comorbid inattentive behaviors is significantly higher than would be expected by chance in samples of individuals with reading difficulties, with 15% to 26% of individuals with a reading disability also meeting criteria for ADHD (Gilger, Pennington, & DeFries, 1992; Shaywitz et al., 1995; Tannock & Brown, 2009; Willcutt & Pennington, 2000).

Behavioral inattention may play a role in reading difficulties by limiting the ability to sustain attention on the text therefore limiting the reader’s ability to comprehend information being read. Symptoms of inattention, as measured by behavioral rating scales, have also been shown to negatively impact behavior and performance, both at home and at school (Flory et al, 2006; Young, Levy, Martin, & Hay, 2009). Children experiencing greater behavioral inattention have been shown to perform more poorly on math and reading achievement tests, even after controlling for confounds such as intelligence (Barriga, Doran, Newell, Morrison, Barbetti, & Robbins, 2002; Grills-Taquechel, Fletcher, Vaughn, Denton, & Taylor, 2013; Roberts, Rane, Fall, Denton, Fletcher, & Vaughn, 2014; Tannock & Brown, 2009). Students with symptoms of behavioral inattention often experience reading difficulties that impede academic performance. Students with reading disabilities have been shown to suffer from deficits in attention that impede reading ability (Flory et al., 2006; Pimperton & Nation, 2010). This is particularly true of those individuals with predominantly inattentive symptoms. Research indicates that the co-occurrence of reading disabilities and ADHD are most likely in those individuals with symptoms of inattention rather than hyperactivity/impulsivity (Carroll et al., 2005; Willcutt, Pennington, Olson, & DeFries, 2007; Willcutt & Pennington, 2000).

As many as 1 in every 20 children in the United States experience symptoms consistent with an ADHD diagnosis (Biederman, 2005). Teacher based rating scales, such as the Strengths and Weaknesses of ADHD symptoms and Normal behavior scale (SWAN), have been shown to be highly reliable at identifying attention problems in children (Coghill & Sonuga-Barke, 2012). The SWAN conceptualizes the Diagnostic and Statistical Manual of Mental Disorders symptom domains of ADHD as a continuum that covers the full range of aptitudes, characterizing the component of the inattention construct as dimensional. Ratings scales such as these are beneficial because teachers are ideal evaluators of behavior being that they are able to observe the behavior of children across multiple settings, over extended periods of time (Evans, Allen, Moore, & Strauss, 2005). Teachers also have a unique normative perspective provided by their interactions with same – aged peers. These types of rating scales produce a much higher incidence of attention deficits, with as many as 17% of students displaying inattentive behavior in the classroom (Young et al, 2006). In addition to developmentally inappropriate levels of behavioral inattention, as many as 40% of students with attention deficits also show evidence of reading difficulties (Carroll, et al., 2005).

While the co-occurrence of ADHD and reading difficulties is high, research typically identifies them as two distinct deficits. Reading disability and behavioral inattention comorbidity occurs more often than chance in both clinic – referred and community samples suggesting that this is not the result of a selection artifact (Willcutt & Pennington, 2000). Additionally, inattention is typically assessed using behavioral ratings, whereas reading disabilities are assessed using cognitive tests. Therefore comorbid reading difficulties and behavioral inattention cannot be explained by shared method variance. Although cognitively and behaviorally dissociable, inattention and reading difficulties have been shown to have very similar underlying neural correlates. For example, recent DTI based studies suggest that white matter tracts associated with reading are also implicated in attention deficits (De La Fuente, Xia, Branch, & Li, 2013; Lawrence et al., 2013). The involvement of overlapping white matter tracts may help to explain the high co-occurrence of behavioral inattention and reading difficulties.

White matter tracts associated with behavioral inattention. Recent DTI based studies suggest relations between symptoms of behavioral inattention and white matter tracts that are also associated with reading, particularly in individuals with ADHD. However, these findings are inconsistent. Numerous studies examining white matter integrity in individuals with ADHD versus controls have found no significant difference in FA values in tracts such as the AF and ILF (Davenport et al., 2008; Lawrence et al., 2013; Pavuluri et al., 2009; Peterson et al., 2011). However, others have found FA values differ in association with ADHD symptoms.

Significantly reduced FA values in the ILF and the AF have been associated with inattentive symptoms in both children and adults with ADHD (De La Fuente, et al., 2013).

Makris et al. (2008) identified significantly lower FA values in the right AF in adults identified (via a behavioral rating scale) as having attention deficits, compared to normal controls. Reduced FA has also been reported in frontal portions of bilateral IFOF in adults with ADHD (Konrad et al., 2010).

Conversely, a relation between increased FA and behavioral inattention has also been suggested. While Konrad et al. (2010) found reduced FA in anterior portions of the IFOF to be associated with symptoms of behavioral inattention; the same study reported increased FA in the UF as well as temporal portions of IFOF, bilaterally. One study, utilizing TBSS methodology, found increased FA values in white matter regions underlying areas associated with the left ILF and UF, as well as the right AF, in children with symptoms of ADHD, as compared to normal controls (Silk, Vance, Rinehart, Bradshaw, & Cunnington, 2009). Measures of right AF integrity have also been shown to be significantly, positively correlated with cognitive measures of inattention in adults with and without attention deficits (Frye et al., 2010; Konrad et al., 2010). Additionally, Konrad et al. (2010) found a positive correlation between FA and scores on an ADHD rating scale but only in typical controls.

Silk et al. (2009) suggested that increased FA in tracts of interest, such as the AF, UF, and IFOF, may indicate white matter abnormalities in children with attention deficits. While several studies support a relation between increased FA and inattention in these tracts, research also suggests a relation between ADHD and reduced FA in portions of the ILF, IFOF, and AF. Further research is needed to examine the relation between behavioral measures of inattention and white matter tract integrity, and how they relate to different aspects of reading proficiency.

Rationale for the Current Study

Researchers have investigated the integrity of the AF, IFOF, ILF, and UF, as they relate differentially to reading difficulties and to behavioral inattention. However, simultaneous examination of the role of each of these tracts and their differential relations to word reading accuracy versus word reading fluency versus reading comprehension has not been completed. Additionally, with overlapping neural correlates, there have been efforts to differentiate between behavioral inattention as a cause of reading difficulties versus the presence of reading disabilities as a comorbid disorder. This literature has typically established disorders of attention, such as ADHD, and reading disabilities as two separable disorders (de Jong et al., 2009; Purvis & Tannock, 2000; Shaywitz, Fletcher, & Shaywitz, 1994) but little is known about white matter microstructure integrity in relation to behavioral inattention in students with and without reading difficulties.

The current study examined white matter tract integrity in four distinct tracts of interest: the AF, IFOF, ILF, and UF and their relation to measures of reading proficiency and behavioral inattention. Specifically, I sought to examine differing relations between tract integrity and measures of word reading accuracy versus word reading fluency versus reading comprehension, as well as behavioral inattention. I hypothesized that each of the four tracts of interest would be differentially associated with components of reading proficiency suggesting a unique role of different white matter tracts in elements of reading. I also expected that these relations would differ in poor readers, as compared to those with typically developing reading skills.

Hypothesis 1, Word reading accuracy: Increased FA values in bilateral AF will be associated with improved word reading accuracy in typical readers but not poor readers.

Hypothesis 2, Word reading fluency: Increased FA values in the left AF, IFOF and ILF will be associated with improved performance on a measure of word reading fluency in typical readers. Alternately, decreased FA values in the right AF and ILF will be related to improved word reading fluency in poor readers.

Hypothesis 3, Reading comprehension: Increased FA values in left ILF and UF will to be associated with the increased reading comprehension ability in both poor and typical readers. Increased FA values in the left ILF and UF will also be associated with increased reading comprehension ability in poor readers but not typical readers.

Hypothesis 4, Inattention: Increased behavioral inattention, as indicated by increased scores on the SWAN teacher rating scale, will be associated with decreased FA values in the left ILF and UF, as well as bilateral AF and IFOF in poor readers.

A unique methodological feature of this study was the use of FA values of tracts which had been residualized in order to represent that which is unique of each tract. White matter tracts commonly overlap in regions where bundles of fibers run parallel. This makes it difficult to assess the unique contribution of these tracts to behavioral outcomes, such as reading proficiency. By comparing "full tract" values to those of a more restrictive tract, which only consisted of those areas that do not contain overlapping tract fibers, the current study was able to better assess the unique relation of each white matter tract to measures of reading proficiency.

Method

Participants

Participants for the current study were recruited from a longitudinal study of reading intervention (Denton et al., 2011; Vaughn, et al. 2010). These participants were those students who had completed all relevant behavioral measures and received structural MRI scans (including a DTI sequence) as part of participation in the intervention studies. Those selected for inclusion in the study had a verbal and/or fluid intelligence score at or above 70 on the *Kaufman Brief Intelligence Test – 2* (Kaufman & Kaufman, 2004), in order to rule out intellectual disabilities. Children with other neurological conditions or diagnosed attention disorders were excluded. Reading group classification was based on students' score on the Letter-Word Identification subtest of the *Woodcock-Johnson III Tests of Achievement* (Woodcock, McGrew, & Mather, 2001). Poor readers were identified as those students who scored below 90 (25^{th} percentile), a common cut point in research studies, indicate problems with single word reading.

All participants were scanned using the same MRI scanner and using the same DTI sequences, as detailed below, approximately 2 years post reading evaluation. Ninety-two participants from the parent study successfully completed a DTI sequence that qualified for inclusion in the current study. Twenty-two participants were excluded because of incomplete behavioral data. DTI data for remaining participants were assessed for quality with five participants excluded for excessive motion and two for poor brain coverage. In all, 63 participants were included in final analysis; 33 poor readers and 30 typical readers.

Measures

Reading measures. As part of the larger studies, each student was administered a series of reading evaluations in a quiet area of his or her school for one or two sessions over a course of one week, by a trained member of the research team, in accordance with standardized task administration procedures. These included individually administered tests of word reading accuracy, fluency, and comprehension.

Word reading accuracy. Word reading skills were assessed using the Letter-Word Identification (LWID) subtest of the *Woodcock-Johnson III Tests of Achievement* (Woodcock et al., 2001). The LWID assesses the ability to accurately read a list of real words. Coefficient alphas based on a large sample from the parent study ranged from 0.93 to 0.97. LWID extended scale score was used as a measure of word reading accuracy.

Word reading fluency. The Sight Word Reading Efficiency subtest of the *Test of Word Reading Efficiency* (TOWRE; Torgesen, Wagner, & Rashotte, 1999) was used to assess reading fluency. The TOWRE measures students' ability to read words out of context. It consists of a timed measure of real word reading, which measures students' ability to recognize common words quickly and accurately. The internal consistency for this well standardized test exceeds 0.95. The total number of words read correctly in the 45 second time limit was used as a measure of word reading fluency.

Reading comprehension. Reading comprehension was assessed using the Passage Comprehension subtest of the *Woodcock-Johnson III Tests of Achievement* (Woodcock et al., 2001). Passage Comprehension assesses the students' language comprehension and reading skills using a cloze procedure. Coefficient alphas based on a large sample from the parent study ranged from 0.93 to 0.97. Passage Comprehension extended scaled score was used as a measure of reading comprehension.

Strengths and Weaknesses of ADHD Symptoms and Normal Behavior Scale. The inattention subscale of the SWAN was used as a measure of behavioral inattention (Swanson et al., 2006). On the nine- item SWAN scale, teachers rated items concerning students' daily activity on a seven-point Likert scale (-3 = far above average; -2 = above average; -1 = somewhat above average; 0 = average; 1 = somewhat below average; 2 = below average; 3 far below average). An individual's total score on the inattention subscale then indicates a measure of attention, with a greater (more positive) score indicating more difficulties with inattention. Comparable to the Disruptive Behavior Rating Scale in reliability (0.82), validity, and heritability, the SWAN is comparably heteroscedastic, making it a preferred measure of positive attention (Arnett et al., 2013).

Magnetic Resonance Imaging

MRI data acquisition. Diffusion-weighted imaging data was collected using a single-shot spin-echo diffusion sensitized echo-planar imaging sequence with an Icosa21 balanced encoding scheme (Hasan & Narayana, 2003). Distortion artifacts were reduced using a SENSE acceleration factor or k-space under-sampling of two (Hasan et al., 2008a). A diffusion sensitization of b=1000 s/ mm^2 and repetition time of 6.1 s and echo time of 84 ms were used. Diffusion weighted image volumes were collected with 21 directions as 44 contiguous 3 mm axial slices with no gap, a square field-of-view 240 mm x 240 mm, and a square image matrix of 256 x 256 pixels (Hasan et al., 2007a; Hasan et al., 2007b). Total DTI acquisition time was approximately 7 minutes.

MRI data processing. DTI data was processed using the FSL package (FMRIB Center, Oxford, United Kingdom). Data from 68 participants was preprocessed including correction for motion and eddy current effects, with data containing motion artifacts excluded from analysis (*n*= 5). FMRIB's Diffusion Toolbox was used to fit the tensor model and to compute FA maps. Voxel – wise analysis was performed using TBSS with the following steps (Smith et al., 2006). All individual FA maps were nonlinearly registered to the FMRIB58_FA standard-space image template and then affine – transformed into standard Montreal Neurological Institute (MNI) space. A mean skeleton map was generated based on the mean FA image of all subjects. The mean FA skeleton represents each tract as a single line with the line running down the center of fiber bundles that are common to all participants. The mean FA skeleton was thresholded at a value of 0.20 to ensure that analysis was restricted to only points within major white matter tracts, which have been successfully aligned across all participants. Voxels with FA < 0.20 were excluded from analysis to avoid partial volume effect from neighboring gray matter. Finally, each subject's aligned FA image was then projected onto the mean FA skeleton, resulting in a skeletonized FA map for each individual, allowing for each participant's FA image to be aligned with the skeleton. This step is performed in order to account for residual local misregistration uncorrected for by nonlinear registration.

Tract based analysis. Tract of interest analysis was performed in order to obtain quantitative DTI indices of tracts hypothesized to be involved in reading: the AF, IFOF, ILF, and UF. White matter tracts of interest were masked bilaterally and symmetrically, utilizing the John Hopkins's University white matter tract atlas in the FMRIB's Diffusion Toolbox. Masks for the IFOF, ILF, and UF were drawn utilizing their respective atlas option. The mask for the AF was drawn utilizing the superior longitudinal fasciculus – main option. Reading performance and behavioral inattention scores were correlated with FA values of the AF, IFOF, ILF, and UF.

Preliminary comparisons revealed an overlap in voxels accounted for by initial tracts (i.e., 36% overlap with left IFOF and left ILF) (see Figure 2). Utilizing the individual tract masks provided by the John Hopkins's University white matter tract atlas, bilateral residualized masks were created by subtracting out all voxels that were also accounted for by an overlapping tract. This provided a mask representing the unique segment of each of the four tracts of interest. FA values for residualized AF, IFOF, ILF, and UF were correlated with reading and behavioral inattention scores.

Statistical analysis

For comparisons of groups**,** traditional t tests and analysis of covariance were conducted using SAS 9.4 statistical software (SAS, 2013). Correlational analyses were done with custom written functions in R Version 3.0.2 (R Development Core Team, 2008). Structure-function relations were estimated using the Pearson correlation, percentage bend and Windersorized correlations, as well as the skipped correlation using the Donoho-Gasko median (DGM). In certain instances, the Pearson correlation can be affected by outliers in the data, thus weakening inferences regarding structure-function relations (Wilcox, 2003). Other robust correlations, included in analyses, are resistant to outliers and therefore provide different conceptualizations of the population. The findings were evaluated in terms of their generalizability across different correlational estimates. Increased reliability of findings was assumed if a pattern of similar coefficients was evident across correlational estimates (Kulesz, Tian, Juranek, Fletcher, & Francis, 2015).

Results

Descriptive Analysis

Table 1 presents descriptive statistics for behavioral measures. Poor and typical reader groups were compared using unpaired t-test to assess for group differences in age and reading ability, as well as behavioral inattention. As expected, groups differed significantly on all measures of reading ability. Groups also differed significantly on age at time of MRI, so age was included as a covariate in group comparisons. Groups did not differ on behavioral inattention. Box-and-whisker plots with Tukey's fencing rule for outlier detection illustrate the presence of univariate outliers in behavioral measures.

Group Comparisons on Tracts of Interest

Tables 2 and 3 present mean FA values for full and residualized measures of white matter tract integrity respectively. Box-and-whisker plots with Tukey's fencing rule for outlier detection illustrate the presence of univariate outliers in FA values for full and residualized tracts (Figures 3 - 6). A one-way analysis of covariance was conducted comparing typical and poor readers on FA values for each of the tracts of interest, controlling for age. There was a significant effect of group on FA in the UF, bilaterally, in both full (right $F(2,59) = 9.88$, $p < 0.001$; left $F(2,59) = 7.18$, $p < 0.001$) and residualized (right $F(2,59) = 10.36$, $p < 0.001$; left $F(2,59) = 6.84$, $p < 0.001$) tracts. No other significant tract differences were present.

Full Tract Analysis

Typical readers. Table 4 presents the single-sample estimates of structure-function relations of full tracts for each of the correlations computed for typical readers. A moderate effect of the relation between reading fluency and right AF was observed in typical readers across estimators, as was evident by the significant percentage bend correlation ($r = 0.37$; $p<$

0.05), with a similar pattern of correlation coefficients across other estimators (*r*= 0.33 – 0.37). A consistent pattern of positive, low-to-moderate correlation coefficients was also observed in relations between reading accuracy and right AF (*r* = 0.18 – 0.22) and behavioral inattention and right UF (r = 0.28 – 0.33).

Poor readers. Tables 5 present single-sample estimates for each of the correlations computed for poor readers. No significant correlations were present in the poor reader group. However, a positive relation between reading comprehension and left ILF showed a pattern of low-to-moderate correlation coefficients (*r* = 0.18 to 0.25).

Residual Tract Analysis

Typical readers. Table 6 presents single-sample estimates for relations between residual tracts and behavioral measures in typical readers. Relations between reading comprehension and left IFOF were significant for the Pearson correlation (*r* = 0.38, $p < 0.05$), but not for the percentage bend, Winsorized or skipped correlations, which may reflect the more robust properties of these estimators. Alternatively, the Pearson correlation for the relation between reading comprehension and left UF was nonsignificant (*r* = -0.24), while the percentage bend correlation had a significant moderate, negative coefficient (*r* = -0.36, $p < 0.05$), with a similar (but nonsignificant) pattern for the Winsorized and skipped using DGM correlations (*r* = -0.32 and *r* = -0.29, respectively). These findings suggest that the robust estimators may better represent the relation between reading comprehension and left UF. Similarly, a significant percentage bend correlation (*r* = 0.37, $p < 0.05$) was observed for the relation between reading fluency and right AF, with a consistent pattern of correlation coefficients for the other three estimators (*r* = 0.33 – 0.37). The relation between word reading accuracy and right AF had a consistent low-to-moderate positive coefficient (*r* = 0.18 to 0.22) across all estimators.

Multiple estimators showed consistent patterns of correlation coefficients for the relation between behavioral inattention and indices of white matter integrity (see Table 6). The relation between behavioral inattention and right UF had a consistent pattern of positive, moderate correlation coefficients (*r* = 0.28 to 0.31). A similar pattern of moderate correlation coefficients was also observed for the relation between inattention and right IFOF.

Poor readers. No significant structure-function relations were observed in poor readers but patterns of correlation coefficients in numerous tracts differed from that of typical readers, as illustrated in Table 7. For instance, there was a pattern of moderate, negative coefficients for robust estimators for the relation between right AF and behavioral inattention (*r* = -0.29 to -0.36). Patterns of moderate, positive coefficients were observed for the relation between reading comprehension and left ILF (*r* = 0.20 to 0.26). A consistent pattern of low, (nonsignificant) negative correlation coefficients was also observed for the relations between word reading accuracy and right ILF (*r* = -0.12 to -0.15), as well as bilateral AF (*r* = -0.11 to -0.19).

These results suggest differing relations between indices of white matter integrity and aspects of reading proficiency and behavioral inattention. Consistent with the hypotheses, results of the current study suggest relations between differing white matter tracts and word reading accuracy versus word reading fluency and reading comprehension. Further, patterns of relations varied between poor and typical readers. Relations between white matter integrity and behavioral inattention were also inconsistent between these groups despite no significant group differences in the measure of behavioral inattention.

Discussion

The current study utilized unique methodology to examine the structure – function relations between white matter microstructural integrity and components of reading proficiency. This technique was also used to assess the relation between behavioral inattention and those tracts associated with reading. These relations were examined in a sample of elementary aged students with typically developing reading skills, as well as a similar sample of poor readers. I hypothesized that the four white matter tracts of interest (i.e., the AF, IFOF, ILF, and UF) would be differentially related to word reading accuracy, word reading fluency, and reading comprehension. Furthermore, it was believed that these relations would differ between poor readers and those students with typically developing reading skills. I also expected that FA values in these tracts would be related to behavioral inattention in poor readers. The results supported differential contributions of the four white matter tracts to different aspects of reading proficiency and behavioral inattention in poor and typical readers.

White Matter Tracts Associated with Reading

Word reading accuracy. Patterns of correlation coefficients for the relations of each aspect of reading and white matter tract integrity varied between reader groups. For example, a pattern suggesting a statistically significant moderate, negative relation between the left UF and word reading accuracy was observed in the students with typically developing reading skills, with lower FA values related to increased word reading accuracy. This relation was not evident in the poor reader group. There was also a consistent pattern of correlation coefficients, across estimators, suggesting a relation between the right AF and word reading accuracy in both typical and poor readers. This is consistent with previous literature (Hoeft et al., 2011; Lebel et al., 2013) and partially supports hypothesis one, in which a relation between bilateral AF and word reading accuracy was expected. Consistent patterns of correlation coefficients were observed for both groups but as hypothesized, these patterns suggested differing relations between good and poor readers. There was a small, negative correlation between the right AF and word reading accuracy in poor readers. Conversely, a stronger, positive (r = 0.22, as opposed to r = -0.12) correlation was observed in typical readers. While there was a relation between the right AF and word reading accuracy in both groups, increased white matter integrity was associated with improved word reading skills in the typical readers. However, decreased integrity was associated with word reading accuracy in the poor readers.

These structure-function relations were similar for both full and residualized tracts. This was to be expected for the AF, as it was the tract with the least amount of overlap with other tracts (3%) and therefore the residualized and full tracts were most similar. These patterns were consistent across estimators, as well as masking methodologies, suggest that the findings are reliable.

Word reading fluency. Poor and typical readers also differed in respect to the relations between word reading fluency and white matter tract integrity. There was a consistent pattern of correlation coefficients suggesting a positive, moderate correlation between fluency and the right AF in typical readers. This suggests that increased white matter integrity in the right AF is associated with increased reading fluency skills in typical but not poor readers. The right UF was the only tract associated with word reading fluency in poor readers, with increased integrity in this tract associated with higher scores on a measure of word reading fluency. A relation between the ILF and word reading fluency was expected (hypothesis two) but was not observed. Previous research (Horowitz-Kraus et al., 2014; Lebel et al., 2013) suggested a contribution of bilateral ILF to reading fluency. However, these studies did not take into account the considerable overlap between the ILF and other tracts, such as the IFOF, also associated with reading. While there was a trend towards a relation between the ILF and fluency, bilaterally, in full tracts for the typical reader group, this pattern was not maintained when the tract was residualized. These findings would suggest that the ILF does not uniquely associate with word reading fluency. Instead, white matter tracts associated with the ventral orthographic route of reading may function together to account for fluency in reading proficiency.

Reading comprehension. A pattern of moderate, negative correlations were observed for the structure-function relation of reading comprehension and the left UF. This relation was evident in the students with typically developing reading skills but not in the poor readers. This suggests that decreased FA values in this tract are associated with reading comprehension skills but only in typical readers.

The pattern of coefficients was not present in the full tract analysis but a reliable pattern was present in the residualized tract analysis. The 65% overlap between the left UF and IFOF could account for the fact that relations could not be detected in the full tract analysis. However, when the IFOF was subtracted out, it was possible to better assess the contribution of the UF to reading comprehension. While previous research has suggested the UF may play a role in language functioning and comprehension (Catani & Mesulam, 2008; Nester et al., 2013), only one study of preterm and typical children and adolescents has shown a significant correlation between the UF and reading comprehension (Feldman et al., 2012). This could be due, in part, to the presence of overlapping fibers from other white matter tracts associated with reading.

Residualized tracts may provide a more accurate representation of that portion of the UF which uniquely contributes to reading comprehension.

Previous research has also indicated a relation between reading comprehension and the ILF (Feldman et al., 2012; Horowitz-Kraus et al., 2014). Similarly, it was believed (hypothesis three) that the left ILF would be associated with reading comprehension in the current study; however no reliable relation was observed. Horowitz-Kraus et al. (2014) found that FA values in the left ILF, as well as bilateral AF, were significantly correlated with a measure of reading comprehension. However, Horowitz-Kraus et al. (2014) did not take the overlapping IFOF into consideration. Like word reading fluency, the contribution the ILF makes to reading comprehension may be better explained by the combination of multiple white matter tracts (e.g. the IFOF and UF) associated with the ventral orthographic route.

White Matter Tracts Associated with Behavioral Inattention

Previous research has suggested a relation between behavioral inattention and white matter tract integrity in those tracts that are also related to reading proficiency but results are inconsistent (e.g., Frye et al., 2010; Konrad et al., 2010; Silk et al., 2009). Some studies find a relation between increased FA and symptoms of inattention (Konrad et al., 2010; Silk et al., 2009), while others found behavioral inattention to be related to reduced FA values in these tracts (Frye et al., 2010; Makris et al., 2008). Only one study examined the relation of white matter integrity and behavioral inattention, as well as elements of reading proficiency, in the same sample (Frye et al., 2010). Frye et al. (2010) was primarily interested in structure - function relations with the AF and IFOF. The contribution of, or overlap with, the ILF was not accessed, despite research suggesting its relation to inattentive behavior (De La Fuente et al., 2013; Silk et al., 2009). Additionally, this was the only study to examine this relation in poor versus typical readers, but no group differences were discussed.

Frye et al. (2010) found no significant relations between inattention and the IFOF; however a reliable pattern of correlation coefficients was observed in the current study, suggesting that increased FA values in the right IFOF was related to increased behavioral inattention. Results of the current study also indicated a positive correlation between behavioral inattention and the right UF. These relations were only observed in typical readers, contrary to the expectation that relations to inattention would be stronger in poor readers. However, this is consistent with one study which found relations between white matter integrity and scores on a measure of behavioral inattention in typical readers but not poor readers (Konrad et al., 2010).

Poor readers displayed a unique relation between white matter integrity and behavioral inattention that was not observed in the typical reader group. The poor reader group showed a pattern of correlation coefficients, across robust estimators, which indicated a moderate, negative correlation between behavioral inattention and FA values in the right AF suggesting that decreased integrity in this tract was associated with increased behavioral inattention in poor readers but not typical readers. This pattern was consistent across masking methodologies. This would suggest that, like reading, the contribution of white matter integrity is differentially related to behavioral inattention in typical versus poor readers. Increased inattention may be related to decreased white matter integrity in poor readers, but not those with typically developing reading skills.

Differing relations between white matter integrity and behavioral inattention in poor and typical readers observed in the current study could help explain the inconsistent results found in previous literature. Traditional research has examined this relation in samples of individuals with ADHD compared to typical controls (Davenport et al., 2009; Konrad et al., 2000; Makris et al., 2008; Pavuluri et al., 2009; Silk et al., 2009). No previous research has accounted for both behavioral inattention and poor reading skills. Instead, individuals with a history of a reading and/or learning disabilities are typically excluded from these studies (e.g., Makris et al., 2008; Peterson et al., 2011). Frye et al. (2010) did account for phonological decoding skills in a group of preterm birth versus typical controls but reading group differences were not assessed.

There is a need for a better understanding of the differing relations of white matter integrity to behavioral inattention in poor versus typical readers, especially because of evidence showing that inattention predicts intervention response and also improves with reading improvement (Roberts et al., 2014). Many children with reading difficulties also exhibit signs of inattention, regardless of whether they meet criteria for ADHD. Behavioral inattention (but not hyperactivity) has also been shown to predict academic performance (Barriga et al, 2002). This might suggest that behavioral inattention impacts reading proficiency differently for those students with co-morbid reading difficulties and ADHD as opposed to those with reading difficulties but no diagnosed attention deficits. It would follow that microstructural integrity in white matter tracts associated with reading and behavioral inattention would also differ in these groups.

While there is little evidence to suggest that behavioral attention interventions are beneficial for promoting reading skills, intensive reading intervention has been shown to improve inattentive behavior in students with reading difficulties (Roberts et al., 2014). Hoeft et al. (2011) found that increased FA in tracts associated with reading proficiency and behavioral inattention was associated with gains in reading ability in poor readers as well as typical readers. This would suggest that intensive reading intervention programs may contribute to microstructural changes in tracts associated with reading and could also account for improvements in behavioral attention. Supporting this, an intensive reading intervention for kindergarteners at risk for reading difficulties was reported to have produced improvements in event-related potentials associated with selective attention (Stevens et al., 2013). Considering the similar white matter tracts associated with both reading and attention, better understanding the observed relations of integrity in these tracts may provide useful insight into the common co-occurrence of reading disabilities and ADHD. It could also help to inform the development of reading intervention programs for those students with reading difficulties and attentional deficits, given that reading interventions have been shown to be successful in improving behavioral attention and underlying neural correlates.

Implications and Future Directions

Current findings highlight the unique relations of the AF, IFOF, ILF, and UF to word reading accuracy versus word reading fluency versus reading comprehension. These finding also suggest that associations between white matter integrity and reading proficiency may differ in poor and typical readers. The reason for these differing associations is unclear. Evidence points to structural variations in brain regions associated with reading, as well as functional abnormalities, in individuals with poor reading skills (Elnakib et al., 2014; Linkersdorfer, Lonnemann, Lindberg, Hasselhorn, & Fiebach, 2012; Maisog, Einbinder, Flowers, Turkeltaub, & Eden, 2008; Richlan, Kronbichler, & Wimmer, 2012). Reduced gray matter has been found in the left superior temporal sulcus and ventral occipitotemporal regions in individuals with poor reading abilities (Richlan et al., 2012). This corresponds with functional neuroimaging studies identifying a left lateralized reading network (Linkerdorfer, 2012; Maisog et al., 2008). In turn, these findings align with DTI studies of poor readers suggesting altered white matter integrity in these regions supporting the reading network. For example, Rimrodt, Peterson, Denckla, Kaufmann, and Cutting (2010) reported reduced white matter integrity in the left inferior frontal gyrus and left temporo-parietal regions. Poor readers often show decreased white matter integrity in bilateral fronto-temporal and left temporo-parietal white matter regions (i.e. AF and ILF) (Carter et al., 2009; Steinbrink et al., 2008; Vandermosten et al., 2012a).

Longitudinal studies suggesting the role of these regions in reading development would also suggest that alterations in typical growth of the developing brain could negatively impact reading. Myers et al. (2014) found that developmental changes in the dorsal temporo–parietal white matter of typically developing kindergarteners was uniquely predictive of reading skills in the third grade. A developmental decrease in grey matter volume in frontal and parietal cortical regions has also been associated with reading proficiency in typically developing children (Houston et al., 2014). Differences in reading ability observed in good versus poor readers could be the result of altered neurodevelopmental changes in brain regions associated with the reading network.

Together, structural and functional neuroimaging studies help identify the neural correlates of reading difficulties. Understanding the contributions of white matter tracts associated with different aspects of reading proficiency could provide insight into microstructural integrity underlying specific reading deficits such as comprehension difficulties in those with typical phonological decoding skills. Future longitudinal studies of white matter maturation in association with reading development are needed to further our understanding of the association between differing white matter tracts and aspects of reading proficiency. This knowledge could be useful in developing a better understanding of those readers who do not respond to typical reading interventions.

Limitations

TBSS methodology was used to obtain FA values as a measure of white matter microstructural integrity in the four tracts of interest. While FA is the most widely used index in brain research (Assaf & Pasternak, 2008), other diffusion – based measures can provide additional information about the directionality, integrity, and functionality of the fibers (Mori, 2007). These include measurements such as overall diffusivity which is commonly quantified using mean diffusivity (Alexander, Lee, Lazar, & Field, 2007). Radial diffusivity is also used as a measure of diffusivity in directions perpendicular to the principal axis of diffusion and is associated with the degree of myelination. Axial diffusivity provides an index of diffusivity along the principal axis and is associated with axon diameter. These diffusion – based measures are not as commonly used but can still provide additional information regarding white matter microstructure that is not obtained by simply utilizing FA as a measure of integrity. However, the value of the information provided by these measures is still relatively unclear, particularly in the typically developing brain.

Another limitation of voxel based approaches such as TBSS lies in the interpretation of cross subject differences in FA in areas of partial volume such as where white matter mixes with grey matter or areas where two or more white matter fiber systems overlap (Assaf & Pasternak, 2008; Smith et al., 2006). The mean FA skeleton is commonly thresholded, typically at 0.2, to account for partial volume where this overlap may occur. However, in smaller tracts, such as the UF, it is difficult to determine whether differences in FA is in fact due to within tract FA changes or if it is related to partial voluming associated with overlapping white matter fibers (Smith et al., 2006). The use of residualized tract masks can reduce this likelihood in voxels specifically identified as containing overlapping white matter tracts but this methodology cannot account for individual differences in those areas identified as "unique" to a given tract. DTI-based tractography is often used as an alternative to voxel based methods but problems with partial voluming still arise in smaller fiber systems and those regions where a considerable overlap of multiple tracts occur, such as those examined here (Assaf & Pasternak, 2008).

The sample of participants utilized in this study presented several limitations. The groups differed significantly on age and IQ. Age was identified as a significant covariate in the majority of group comparisons of tract integrity but was not accounted for in the structure – function correlational analyses. Because of this, relations observed in the older poor reader group might be attributed to changes in FA associated with development. This is particularly true given that poor and typical readers exhibit different developmental trajectories in brain regions associated with reading (Houston et al., 2014). There was also a significant group difference in IQ, with poor readers scoring lower on verbal and/or performance IQ. However, current views question the relevance of IQ in identifying individuals with reading difficulties (Francis, Fletcher, Stuebing, Lyon, Shaywitz, & Shaywitz, 2005) and has not been shown to affect the activation profiles of brain regions associated with reading (Simos, Rezaie, Papanicolaou, & Fletcher, 2014) and therefore was not a central question of this study.

Although groups differed significantly on all measures of reading, the current study identified poor readers as those with lower word reading skills. Additional research is needed to assess the relation of white matter integrity to reading proficiency in individuals with reading difficulties not associated with word reading deficits. Additionally, only those students without a formal ADHD diagnosis were included in this study. Doing so may have eliminated potential participants with the most severe attentional deficits and thus limiting the ability to detect a relation between white matter integrity and behavioral inattention. However, the use of a teacher rating scale, such as the SWAN, has been shown to produce higher incidence of attention deficits (Young et al., 2006) and scores on this measure of behavioral inattention were evenly distributed in the current sample. This allowed the current study to be more representative of the typical classroom, despite the exclusion of children with identified attention disorders.

I utilized robust estimators in the single sample assessment of structure – function relations. The use of bootstrapping statistics with these estimators can provide a more representative estimation of population correlations. The small sample size of the current study did not allow for this. Future studies would benefit from the use of these techniques in order to obtain a more complete understanding of the relation of white matter microstructural integrity to reading proficiency and behavioral inattention.

Conclusion

Components of reading proficiency such as reading accuracy, fluency, and comprehension require the successful coordination of numerous, yet distinct, cortical regions. Underlying white matter tracts such as the AF, IFOF, ILF, and UF allow for the successful communication between these regions. To the extent that different reading processes require activation and communication between differing regions, then it may also follow that differing white matter tracts may be related to different aspects of reading proficiency. This study identified the unique relation of white matter microstructure to word reading accuracy versus word reading fluency versus reading comprehension, as well as behavioral inattention. Additionally, differing relations were observed in poor readers and those students with typically developing reading skills. These findings expand our understanding of white matter microstructure as it relates to different aspects of reading proficiency. Reduced integrity in these tracts could underlie specific reading deficits, as well as the presence of co-morbid attention deficits.

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Table 1

Descriptive statistics for behavioral measures for typical and poor readers.

Variable	Typical (n = 30) *M(SD)*	Poor (n = 33) *M(SD)*	t	p	*Cohen's d*
Age	10.51 (2.90)	12.27 (2.63)	-2.52	0.01	-0.63
Accuracy	102.20 (8.28)	76.82 (11.16)	10.16	< 0.001	2.60
Comprehension	95.11 (9.63)	77.24 (11.38)	6.94	< 0.001	1.76
Fluency	97.73 (8.40)	81.27 (14.17)	5.54	< 0.001	1.41
Inattention	2.63 (14.14)	-2.52 (9.91)	1.69	0.10	0.42

Note. *M* = mean; *SD* = standard deviation

Table 2

Fractional anisotropy values for full tracts for typical and poor readers.

Tract	Typical (n = 30) *M(SD)*	Poor (n = 33) *M(SD)*	F(3,59)	p	*Cohen's d*
Right AF	0.47 (0.02)	0.48 (0.02)	2.36	0.08	0.06
Right IFOF	0.53 (0.02)	0.53 (0.03)	1.34	0.27	0.02
Right ILF	0.52 (0.02)	0.52 (0.03)	0.73	0.54	0.02
Right UF	0.48 (0.03)	0.49 (0.03)	9.88	< 0.001	0.06
Left AF	0.47 (0.02)	0.47 (0.02)	1.45	0.24	0.05
Left IFOF	0.53 (0.02)	0.53 (0.03)	2.19	0.10	0.04
Left ILF	0.51 (0.02)	0.52 (0.02)	0.72	0.54	0.03
Left UF	0.49 (0.02)	0.49 (0.03)	7.18	< 0.001	0.04

Note. *M* = mean; *SD* = standard deviation; AF = arcuate fasciculus; IFOF = inferior fronto – occipital fasciculus; ILF = inferior longitudinal fasciculus; UF = uncinate fasciculus.

Table 3

Fractional anisotropy values for residualized tracts for typical and poor readers.

Tract	Typical (n = 30)	Poor (n = 33)	F(3,59)	p	*Cohen's d*
	M(SD)				
Right AF	0.47 (0.02)	0.48 (0.02)	2.36	0.08	0.06
Right IFOF	0.51 (0.02)	0.51 (0.02)	1.30	0.28	0.02
Right ILF	0.46 (0.02)	0.47 (0.02)	0.61	0.61	0.03
Right UF	0.48 (0.03)	0.49 (0.03)	10.36	< 0.001	0.07
Left AF	0.47 (0.02)	0.47 (0.02)	1.41	0.25	0.05
Left IFOF	0.49 (0.02)	0.49 (0.03)	1.77	0.16	0.03
Left ILF	0.47 (0.02)	0.47 (0.02)	0.34	0.80	0.02
Left UF	0.48 (0.03)	0.49 (0.03)	6.84	< 0.001	0.05

Note. M = mean; SD = standard deviation; AF = arcuate fasciculus; IFOF = inferior fronto – occipital fasciculus; ILF = inferior longitudinal fasciculus; UF = uncinate fasciculus.

Table 4

Single sample estimates of population correlation relations for full tracts in typical readers.

Pair of Variables	Pearson Correlation	Skipped Correlation using DGM	Percentage Bend Correlation	Winsorized Corrleation
Accuracy –Right AF	*0.22*	*0.18*	*0.21*	*0.22*
Accuracy -Right IFOF	0.10	-0.13	-0.01	-0.001
Accuracy –Right ILF	0.15	-0.04	0.04	-0.004
Accuracy –Right UF	-0.13	-0.24	-0.21	-0.21
Accuracy –Left AF	0.11	-0.03	0.07	0.05
Accuracy –Left IFOF	0.09	-0.13	-0.02	-0.08
Accuracy –Left ILF	0.19	0.03	0.08	0.08
Accuracy –Left UF	-0.16	-0.29	-0.30	-0.35
Comprehension –Right AF	0.18	0.18	0.11	0.08
Comprehension -Right IFOF	0.23	0.23	0.05	0.09
Comprehension –Right ILF	0.17	0.17	0.01	-0.08
Comprehension –Right UF	-0.11	-0.22	-0.17	-0.15
Comprehension –Left AF	0.11	0.11	0.02	-0.02

Comprehension –Left IFOF	0.27	0.09	0.13	0.11
Comprehension –Left ILF	0.21	0.21	-0.01	-0.07
Comprehension –Left UF	-0.03	-0.13	-0.09	-0.07
Fluency –Right AF	*0.33*	*0.37*	***0.37***	*0.35*
Fluency -Right IFOF	0.09	0.19	0.08	0.02
Fluency –Right ILF	*0.11*	*0.11*	*0.11*	*0.13*
Fluency –Right UF	0.10	0.15	0.02	-0.03
Fluency –Left AF	0.25	0.37	0.30	0.28
Fluency –Left IFOF	0.06	0.06	0.10	0.03
Fluency –Left ILF	0.16	0.30	0.19	0.19
Fluency –Left UF	0.14	0.18	-0.002	-0.10
Inattention –Right AF	*0.17*	*0.17*	*0.14*	*0.12*
Inattention-Right IFOF	0.26	0.26	0.18	0.21
Inattention –Right ILF	0.24	0.24	0.19	0.16
Inattention –Right UF	*0.29*	*0.29*	*0.28*	*0.33*
Inattention –Left AF	0.13	0.13	0.11	0.07
Inattention –Left IFOF	0.19	0.19	0.14	0.18

Inattention –Left ILF	0.19	0.19	0.12	0.05
Inattention –Left UF	0.13	0.13	0.20	0.27

Note: N = 30; **Bolded** = statistically significant results based on $p < 0.05$.; *Italicized* = pattern of correlation coefficients across estimators. AF = arcuate fasciculus; IFOF = inferior fronto – occipital fasciculus; ILF = inferior longitudinal fasciculus; UF = uncinate fasciculus.

Table 5

Single sample estimates of population correlation relations for full tracts in poor readers.

Pair of Variables	Pearson Correlation	Skipped Correlation using DGM	Percentage Bend Correlation	Winsorized Corrleation
Accuracy –Right AF	-0.11	-0.11	-0.11	-0.12
Accuracy -Right IFOF	>0.001	>0.001	0.06	0.10
Accuracy –Right ILF	-0.07	-0.06	0.004	-0.03
Accuracy –Right UF	>0.001	-0.13	0.02	0.07
Accuracy –Left AF	*-0.16*	*-0.16*	*-0.14*	*-0.18*
Accuracy –Left IFOF	-0.04	-0.04	0.01	0.01
Accuracy –Left ILF	*0.05*	*0.05*	*0.08*	*0.07*
Accuracy –Left UF	-0.03	0.06	0.02	0.03
Comprehension –Right AF	>0.001	>0.001	0.01	0.03
Comprehension -Right IFOF	0.02	0.02	0.07	0.12
Comprehension –Right ILF	-0.11	-0.04	0.01	0.003
Comprehension –Right UF	0.03	>0.001	0.03	0.06
Comprehension –Left AF	*-0.05*	*-0.04*	*-0.04*	*-0.02*

Comprehension –Left IFOF	0.10	0.12	0.21	0.24
Comprehension –Left ILF	*0.20*	*0.18*	*0.22*	*0.25*
Comprehension –Left UF	0.04	0.09	0.14	0.16
Fluency –Right AF	0.08	0.07	0.12	0.13
Fluency-Right IFOF	0.15	0.15	0.26	0.34
Fluency –Right ILF	-0.09	0.05	0.16	0.16
Fluency –Right UF	0.23	0.15	0.20	0.23
Fluency –Left AF	-0.05	-0.09	0.07	0.07
Fluency –Left IFOF	0.17	0.18	0.28	0.27
Fluency –Left ILF	0.12	0.15	0.24	0.27
Fluency –Left UF	0.23	0.13	0.23	0.26
Inattention –Right AF	-0.13	-0.35	-0.29	-0.30
Inattention-Right IFOF	-0.05	-0.14	-0.12	-0.12
Inattention –Right ILF	-0.09	-0.04	-0.05	-0.13
Inattention –Right UF	0.06	-0.12	-0.05	-0.16
Inattention –Left AF	-0.17	-0.31	-0.20	-0.17
Inattention –Left IFOF	-0.17	-0.21	-0.19	-0.25
Inattention –Left ILF	-0.12	-0.13	-0.11	-0.19

Inattention –Left UF	0.16	-0.10	-0.09	-0.23

Note: N = 30; **Bolded** = statistically significant results based on p < 0.05.; *Italicized* = pattern of correlation coefficients across estimators. AF = arcuate fasciculus; IFOF = inferior fronto – occipital fasciculus; ILF = inferior longitudinal fasciculus; UF = uncinate fasciculus.

Table 6

Single sample estimates of population correlation relations of residualized tracts in typical readers.

Pair of Variables	Pearson Correlation	Skipped Correlation using DGM	Percentage Bend Correlation	Winsorized Correlation
Accuracy –Right AF	*0.22*	*0.18*	*0.22*	*0.22*
Accuracy -Right IFOF	0.11	-0.11	-0.001	-0.01
Accuracy –Right ILF	0.17	0.03	0.08	0.07
Accuracy –Right UF	-0.08	-0.17	-0.15	-0.14
Accuracy –Left AF	0.10	-0.03	0.07	0.04
Accuracy –Left IFOF	0.11	-0.13	0.01	-0.01
Accuracy –Left ILF	0.27	0.10	0.17	0.15
Accuracy –Left UF	-0.20	-0.29	-0.32	-0.32
Comprehension –Right AF	0.17	0.17	0.11	0.08
Comprehension -Right IFOF	0.28	0.10	0.10	0.13
Comprehension –Right ILF	0.21	0.21	0.10	0.04
Comprehension –Right UF	-0.07	-0.18	-0.13	-0.13
Comprehension –Left AF	0.10	0.10	0.03	-0.02

Comprehension –Left IFOF	**0.38**	0.20	0.26	0.27
Comprehension –Left ILF	0.31	0.31	0.11	0.05
Comprehension –Left UF	-0.24	*-0.35*	***-0.36***	*-0.36*
Fluency –Right AF	*0.33*	*0.37*	***0.37***	*0.35*
Fluency-Right IFOF	0.11	0.23	0.09	0.03
Fluency –Right ILF	0.20	0.20	0.23	0.26
Fluency –Right UF	0.10	0.14	0.02	-0.05
Fluency –Left AF	0.24	0.36	0.29	0.28
Fluency –Left IFOF	0.04	0.17	0.07	0.04
Fluency –Left ILF	0.27	**0.46**	0.34	0.34
Fluency –Left UF	0.03	0.05	-0.06	-0.09
Inattention –Right AF	0.17	0.17	0.14	0.11
Inattention -Right IFOF	*0.20*	*0.20*	*0.16*	*0.19*
Inattention –Right ILF	*0.13*	*0.13*	*0.17*	*0.16*
Inattention –Right UF	*0.29*	*0.30*	*0.28*	*0.31*
Inattention –Left AF	*0.11*	*0.11*	*0.11*	*0.07*
Inattention –Left IFOF	0.09	0.09	0.07	0.15
Inattention –Left ILF	*0.10*	*0.10*	*0.10*	*0.09*

Inattention –Left UF	0.01	0.01	-0.06	-0.06

Note: N = 30; **Bolded** = statistically significant results based on $p < 0.05$.; *Italicized* = pattern of correlation coefficients across estimators. AF = arcuate fasciculus; IFOF = inferior fronto – occipital fasciculus; ILF = inferior longitudinal fasciculus; UF = uncinate fasciculus.

Table 7

Single sample estimates of population correlation relations for residualized tracts in poor readers.

Pair of Variables	Pearson Correlation	Skipped Correlation using DGM	Percentage Bend Correlation	Winsorized Correlation
Accuracy –Right AF	*-0.11*	*-0.11*	*-0.12*	*-0.12*
Accuracy -Right IFOF	0.01	0.01	0.04	0.07
Accuracy –Right ILF	*-0.14*	*-0.15*	*-0.12*	*-0.14*
Accuracy –Right UF	0.05	-0.09	0.08	0.06
Accuracy –Left AF	*-0.17*	*-0.17*	*-0.15*	*-0.19*
Accuracy –Left IFOF	-0.04	-0.10	-0.04	-0.03
Accuracy –Left ILF	0.10	0.07	0.06	0.04
Accuracy –Left UF	0.01	-0.01	0.03	0.03
Comprehension –Right AF	>0.001	>0.001	0.01	0.03
Comprehension -Right IFOF	0.02	0.02	0.08	0.16
Comprehension –Right ILF	-0.11	-0.11	-0.04	-0.04
Comprehension –Right UF	*0.03*	*0.03*	*0.04*	*0.02*
Comprehension –Left AF	*-0.05*	*-0.05*	*-0.05*	*-0.02*

Comprehension –Left IFOF	0.10	0.10	0.19	0.23
Comprehension –Left ILF	*0.20*	*0.20*	*0.24*	*0.26*
Comprehension –Left UF	*0.04*	*0.04*	*0.04*	*0.02*
Fluency –Right AF	0.08	0.07	0.12	0.13
Fluency -Right IFOF	0.15	0.14	0.26	0.34
Fluency –Right ILF	-0.09	-0.09	0.01	0.05
Fluency –Right UF	*0.23*	*0.23*	*0.23*	*0.25*
Fluency –Left AF	-0.04	-0.09	0.06	0.07
Fluency –Left IFOF	0.17	0.13	0.24	0.25
Fluency –Left ILF	0.12	0.14	0.21	0.24
Fluency –Left UF	0.23	0.11	0.20	0.21
Inattention –Right AF	-0.13	*-0.36*	*-0.29*	*-0.30*
Inattention -Right IFOF	-0.05	-0.23	-0.19	-0.20
Inattention –Right ILF	-0.09	-0.19	-0.13	-0.22
Inattention –Right UF	0.06	-0.14	-0.05	-0.16
Inattention –Left AF	-0.17	-0.32	-0.20	-0.18
Inattention –Left IFOF	-0.17	-0.27	-0.28	-0.35
Inattention –Left ILF	-0.12	-0.23	-0.20	-0.26

Inattention –Left UF	0.16	-0.04	0.02	-0.11

Note: N = 30; **Bolded** = statistically significant results based on p < 0.05.; *Italicized* = pattern of correlation coefficients across estimators. AF = arcuate fasciculus; IFOF = inferior fronto – occipital fasciculus; ILF = inferior longitudinal fasciculus; UF = uncinate fasciculus.

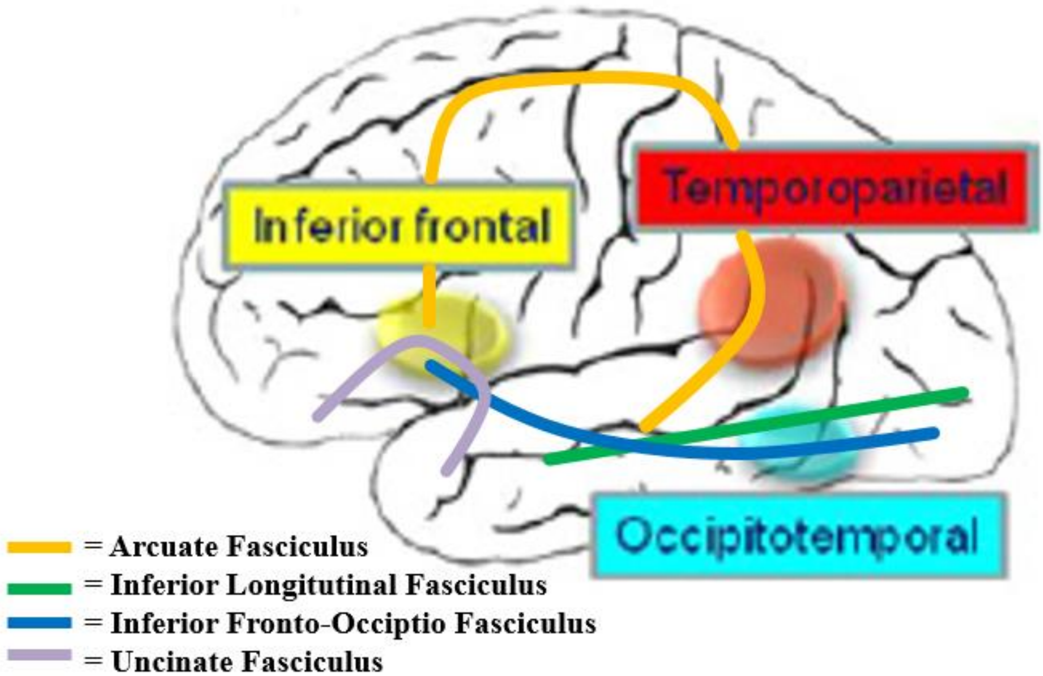

Figure 1. Network of white matter tracts associated with reading proficiency and behavioral inattention.

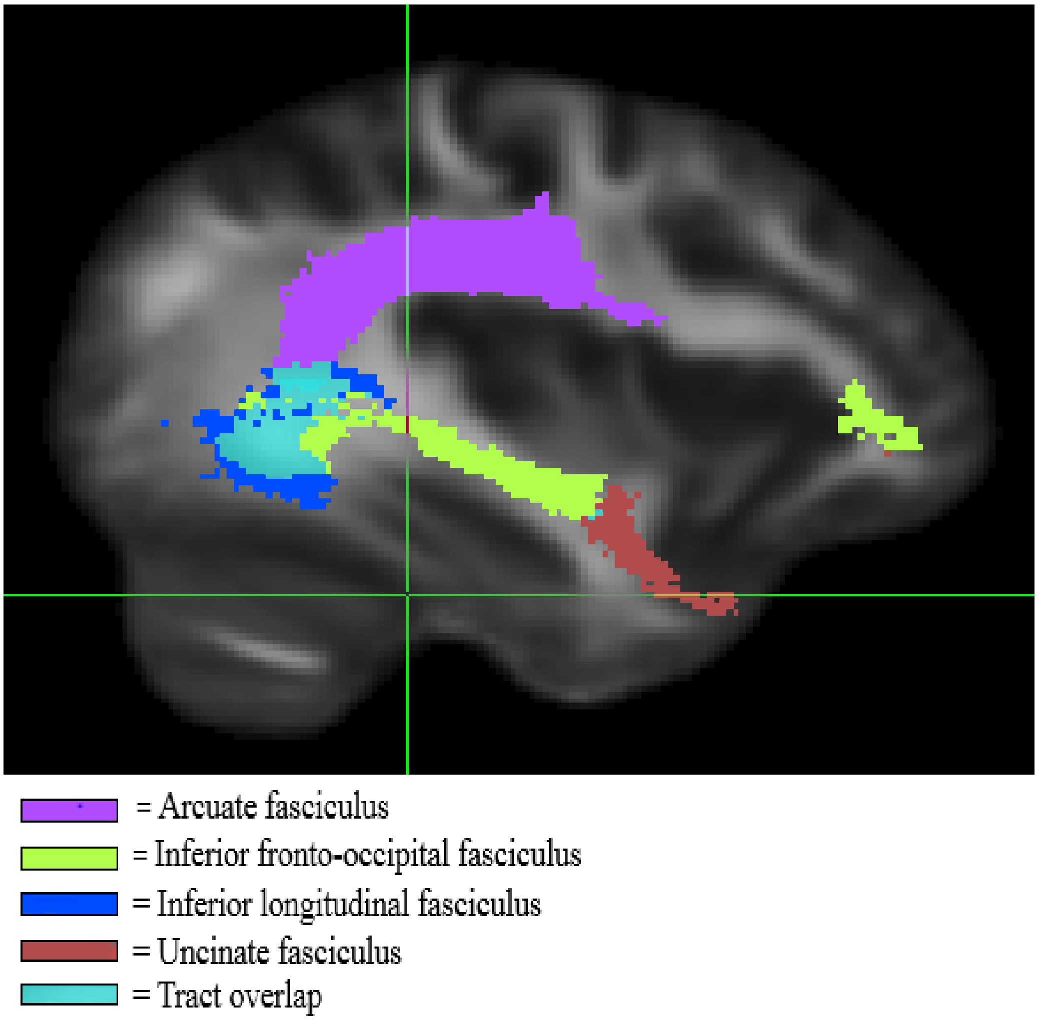

Figure 2. Masks utilized for tracts associated with reading and behavioral inattention. Masking in teal demonstrates a 36% overlap between the left inferior fronto-occipital fasciculus and the left inferior longitudinal fasciculus which was subtracted out during the residualization process.